REMARKS

Withdrawn Claims

Applicants request that withdrawn claims 41 and 42 be considered in this application. These claims are directed to compounds that are claimed more broadly in claim 37, which is being considered. There is no rationale provided for not considering these claims; and there may be none since their subject matter must have been considered when examining claim 37.

Double Patenting Rejections

Applicants will attend to the merits of provisional rejections under double patenting if any maintained once allowable subject matter is identified.

Nevertheless, applicants point out that the double patenting rejections over US 08/995,750 and US 08/996,343 are improper since these applications are no longer co-pending. US 08/995,750 and US 08/996,343 were converted into provisional applications 60/126,434 and 60/135,501, respectively, which are now abandoned, e.g., more than 1 year passed since conversion of these applications into provisional applications. Thus, these references are neither patents nor pending applications over which proper double patenting rejections can be made.

The Rejection Under 35 USC § 112, first paragraph

Claims 1, 9, 11, 12, 13, 15 and 16 were rejected as allegedly not enabled because the substituent group R1 is defined as a C1-13 heteroaryl moiety.

This rejection does not appear to apply to claims 11, 12, 15, and 16. Claims 12 and 16 define R1 as t-butyl only and claims 11 and 15 are directed to specific compounds that were prepared and tested for activity. See specification.

Claims 1, 9 and 13, are directed to a method of treating cancerous cell growth with compounds of formula I, where substituent R1 may be a heteroaryl moiety.

The Office Action admits that the specification provides guidance on pages 112 to 114 for raf Kinase assays of the compounds. Nevertheless the Office Action alleges that it would pose undue experimentation in regards to the treatment of all cancerous cell growth, etc. These statements are contradictory. The specification provides guidance to one of ordinary skill in the art on how to test the raf kinase activity of the claimed compounds. One of ordinary skill in the art can, without undue experimentation, assay thousands of the claimed compounds, including compounds having a variety of heteroaryl groups, which are

finite (the number of possible specific heteroaryl groups claimed generally are finite) for raf kinase activity. Additionally, the state of the art related to cancer treating pharmaceuticals is at a stage where numerous assays/screening protocols/cancer models are known in the art in which the activity of the claimed compounds can be tested for a variety of cancers. Just because the number of possible compounds may be large that have a heteroaryl group as R1 and that there are numerous types of cancers, it does not mean that it would pose undue experimentation to practice the claimed invention. Testing of thousands of compounds in various assays in the field of pharmaceutical inventions is routine.

> With the arrival of robotics and with miniaturization of *in vivo* testing methods, it became possible in the 1980s ... to screen thousands of compounds on a large number of biological targets. ... As it is now possible for a pharmaceutical company to screen several thousand molecules simultaneously in 30 to 50 different biochemical tests.

See Camille Georges Wermuth, The Practice of Medicinal Chemistry, Academic Press, 1996, fourth printing 2001, page 86.

> Automation is required at all stages of the pharmaceutical, chemical and biotechnological discovery, development and manufacturing process in order to achieve increased speed and throughput. Large synthesis facilities exist for combinatorial chemistry programs to deliver thousands up to hundreds of thousands of compounds for mass screening. ... High throughput screening ... enable[s] the [testing of the] target number of 100,000 compounds per day at affordable costs.

See Heinrich Klefenz, Industrial Pharmaceutical Biotechnology, WILEY-VCH Verlag GmbH, 2002, p. 172.

With the state of the art being at the stage as described in the above cited books there is no basis for a rejection for lack of enablement in a case where applicants provide guidance as to how the activity of the compounds may be tested. At this point it takes merely routine testing/screening, which is not undue experimentation, to determine the activity level of a variety of compounds within the claims.

Additionally, applicants even provide activity data for two compounds (compounds number 287 and 385) that have a heteroaryl group as R1. See specification page 101, 110 to 112.

Applicants provided adequate guidance to those of ordinary skill in the art how to test the claimed compounds and provided examples to the use/activity of the claimed compounds. Providing more is not necessary to enable the claimed invention.

Even absent guidance as to how to test the activity of the compounds and examples

demonstrating activity, the courts have placed the burden upon the PTO to provide **evidence or reason** shedding doubt on the disclosure that the invention can be used as stated; see, e.g., *In re Marzocchi*, 439 F.2d 220, 169 USPQ 367 (CCPA 1971) (Holding that how an enabling teaching is set forth, either by use of illustrative examples or by broad terminology, is of no importance.) No such evidence or reason for doubting Applicants' disclosure is provided.

The MPEP is also in accord with this as it states that "compliance with the enablement requirement of 35 U.S.C. 112, first paragraph, does not turn on whether an example is disclosed." See MPEP § 2164.02.

The PTO has failed to meet its burden. No evidence or reason has been presented which would demonstrate that the guidance provided by the specification is inadequate to enable the testing of the claimed compounds without undue experimentation.

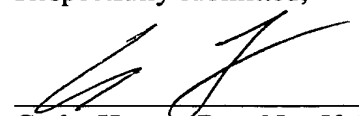
With regard to *Wands*, supra, used by the Examiner as the basis of the rejection, the court therein teaches that whether undue experimentation is needed is not a single, simple factual determination, but rather is a conclusion reached by weighing many factual considerations. The court in *Wands*, further held that the test is not merely quantitative, since a **considerable amount of experimentation is permissible, if it is merely routine, or if the specification in question provides a reasonable amount of guidance with respect to the direction in which the experimentation should proceed**.

The citations from the books demonstrate that testing/screening/assaying compounds in the pharmaceutical industry is merely routine. Applicants also provided guidance as to which direction the testing should proceed. Additionally, the state of the art of cancers is such that one of ordinary skill in the art can select numerous known assays/cancer models representing different types of cancers, and test the claimed compounds in such assays/cancer models. Thus, under *Wands*, these rejections cannot be maintained.

Applicants submit that the entire scope of the claims is enabled for the reasons discussed above.

The Commissioner is hereby authorized to charge any fees associated with this response or credit any overpayment to Deposit Account No. 13-3402.

Respectfully submitted,



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